

Clinical Pathologist's Chair

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Monoclonal antibodies

Antibodies are immunoglobulins produced by the B-lymphocytes when an animal is immunized with an antigen. The different clones of B-lymphocytes produce a variety of antibodies that have multiple specificities, even when a pure antigen is used, and this mixture of antibodies is referred to as polyclonal. Since these polyclonal antibodies can react with many antigens, they require extensive purification before being used in diagnostic procedures.

Monoclonal antibodies, in contrast

to the polyclonal type, are directed against a single antigenic determinant. Their production is based on the hybridoma technology¹. Hybridoma is the name of the hybrid product of an antibody producing B-lymphocyte and a mouse myeloma cell. A single clone of cells that produces an immunoglobulin specific for a unique antigen is isolated, harvested and fused with a malignant lymphocyte from a mouse myeloma. The hybrid produced by these 2 cells has properties of both cells. The myeloma cell is a mutated cell that has lost its ability to produce myeloma immunoglobulins but confers an exaggerated cell proliferative ability and the cloned B-lymphocyte confers the ability to produce a specific antibody. The hybrid cells are maintained in culture and produce a specific antibody that reacts with the specific antigen or antigenic determinant (epitope) that had stimulated its formation.

A monoclonal antibody from a given clone is essentially homogenous, is easier to characterize and has a more repro-

ducible behavior than the polyclonal antibodies. The advantages of monoclonal over the polyclonal antibodies are their increased specificity and the ability to produce large quantities from an isolated hybridoma clone. Some disadvantages include the high cost of production and the intensive labor required in the initial identification of the ideal B-lymphocyte clone and the frequent low affinity of the monoclonal antibodies.

Monoclonal antibodies were first used in the cellular phenotyping of hematopoietic cell surface markers; but they are now also used to study autoimmune diseases, infectious diseases, cancer and the assay of various substances. The cellular phenotyping of hematopoietic cell surface markers is important in the diagnosis of the leukemias and lymphomas, and the characterization of the immune deficiency diseases. The first useful reagents were those that defined the T-lymphocyte. Before monoclonal antibodies became available, human T-cells were identified on the basis of

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Liberator/ Stroller

Portable Liquid Oxygen
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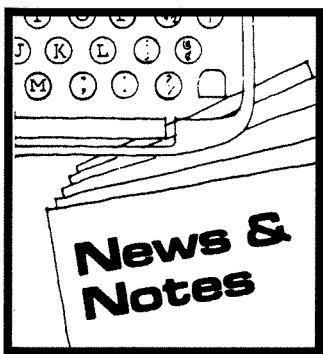
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Henry N. Yokoyama MD

Letter From a Dear Friend

22 June 1991

Harry L. Arnold, Jr., MD
250 Laurel Street, #301
San Francisco, CA 94118

Dear Henry:

What a heartwarming idea, to have a semicentennial celebration for the Journal! I am grieved to be unable to accept it — and I'll still show up if my situation changes; but at the moment this seems very unlikely. I've had one course of radiation therapy and still have painful consequences and only partial evidence of success — and they will consider repeating it in 2 or 3 weeks. I hope I'll make it in September, but I really don't expect to.

It was a great pleasure and privilege to have you as a member of the editorial staff with your lively readable Notes & News all those years, Henry! Any editor should be so blessed! I'm very glad indeed that you decided to stay on the job; thank you again and again!

Warmest regards!
Harry

Life in These Parts

LEECHES? Straub surgeon Randy Wong became the first in Hawaii to use imported leeches to decongest a myocutaneous flap on a postop oral cancer patient. Randy, while an assistant professor at Pennsylvania State University Hospital, had used leeches in surgery, but the State Department of Agriculture expressed concern. With the advent of microsurgery and myocutaneous flaps, Randy has seen a resurgence of the use of leeches in the past decade...

SODA CAN PULL TABS HELP PAY FOR DIALYSIS? Someone asked *Kokua Line* if this was true. "Dick Goad, manager of St Francis Hospital's Renal Institute told *Kokua Line* that no renal program in the nation accepts flip tops in exchange for dialysis treatment. 'Reports that flip tops help dialysis patients is a malicious rumor that gets resurrected every several years'."

TB CASES: Richard Frankel, chief of the Tuberculosis/Hansen's Disease Control Branch of Hawaii reports the total number of TB cases for 1990 as 196 — the largest of any year since 1984. Of the 196 cases, 165 (84.2%) occurred in foreign-born immigrants to Hawaii. Richard predicts that the number of cases will increase in the coming years because of increased immigration from

high prevalence countries authorized under the Immigration Act of 1990.

HAWAIIAN HEALTH FAIR: The 2nd annual Hawaiian health fair was held on May 4th in Hilo, chaired by A. Scott Miles. The goals were to increase health knowledge, perform diagnostic screening and encourage health and fitness among Hawaiians. Seminars were conducted by Terry Shintani, Mans Ghosh, John Uohara, Gerrit Ludwig, Henry Yang, Lambert Lee Loy and Henry Lee Loy...

Conference Humor

Back in Ireland when I was a medical student, we sat in alphabetical order in the classroom. Being a Ryan, I sat in the back row and couldn't see or hear too well from there. So when we got to the hospital, I took a seat up front. The surgical professor was a Mr O'Connel. That first day, he looked at me and asked, "What's your name?" "Ryan, sir." "Well Mr Ryan, will you explain to the class the causes of ulcerative colitis." We hadn't covered the subject so I replied, "I don't know sir." Mr O'Connel admonished, "Don't say you don't know ... Say you've forgotten."

Several weeks later, we were back at the hospital. Mr O'Connel remembered me. "Mr Ryan, isn't it? Well, Mr Ryan, will you tell the class the cause of Hashimoto's Thyroiditis." "I'm sorry sir ... I've forgotten," I replied. Wherein Mr O'Connel remarked, "Witness one of the tragedies of our times. No one knows the cause of Hashimoto's Thyroiditis and here is a medical student who has forgotten"

(As told by VP Colman Ryan, UCSF)

Hors de Combat

A telephone survey of 150 physicians, aged 58 or older, in all 50 states by Merritt, Hawkins and Associates, physician search consultants of Irvine, Calif revealed the following: 68% feel that the practice of medicine has become less satisfying in the last 5 years.

41% would choose a field other than medicine if they could choose again.

58% would not encourage a son or daughter to enter the medical profession.

64% identify government intervention as the greatest cause of their frustration.

Elected, Appointed & Honored

St Francis Hospital installed Kenneth Ing president and chief of staff; Paul DeMare VP; Arnold Siemsen secretary; and Glenn Pang treasurer. Thomas Tasaki was elected member-at-large to the executive board. William Dang Jr is the new chief of cardiology, Michael Imura is chief of psychiatry and Jorge Camara is chief of ophthalmology.

Of Lawyers and Men

"You have a gun with only two bullets. You are cornered in a small room with the following dangerous species: a lawyer, a snake, and Saddam Hussein. How should you use the two bullets to best protect yourself?" Answer: "Shoot the lawyer twice..."

(As told by our tennis-playing lawyer friend Rick Turpin)

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CLINICAL PATHOLOGIST'S CHAIR(Continued from page 288)

their ability to bind sheep red blood cells to form E-rosettes. A series of monoclonal antibodies can define the various T-cell subsets such as the T-helper inducer and T-cytotoxic suppressor cell. Also available are the antibodies against the B-cell, common leukocyte, monocytes and granulocytes.

Monoclonal antibodies have been used to subclassify non-Hodgkins lymphomas and phenotype the acute lymphoblastic leukemias. Flow cytometry is the most commonly used method for assaying the surface antigen expression of many individual cells. The cells with surface antigens are labeled with a fluorochrome conjugated monoclonal antibody, drawn into the cytometer and quantitated.

Monoclonal antibodies have been developed for identifying various infectious agents: Bacterial antibodies (eg, *Clostridium difficile*, *Legionella pneumophila* and *Neisseria*); viral antibodies (eg, Cytomegalovirus, hepatitis A and B and varicella-zoster); parasitic

antibodies (eg, *cryptosporidium* and *toxoplasma*); and fungal (eg, *Candida albicans*). Some of these monoclonal antibodies have replaced conventional and microbiological methods because of improved sensitivity, specificity and speed².

Monoclonal antibodies are also used in the assay of hormones such as human chorionic gonadotropin, TSH, growth hormone, prolactin and thyroid hormones. There are ongoing studies of how to conjugate radioactive agents to image tumors and metastases, immunotherapy with monoclonal antibodies and therapy with cytotoxic agents that are attached to monoclonal antibodies against tumors.

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1. Kohler, G & Milstein, C. Continuous cultures of fused cells secreting antibody of predefined specificity, *Nature* (London) 256:495-497, 1975.
2. Fung, JC and Tilton, RC. Rapid methods for detecting infectious diseases, *Lab Med* 18:74-76, 1987.